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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/319,724	09/08/1999	GERLINDE LENZEN	045636-5025	3497

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EXAMINER

BRANNOCK, MICHAEL T

ART UNIT	PAPER NUMBER
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1646

DATE MAILED: 03/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/319,724

Applicant(s)

Lenzen et al.

Examiner

Michael Brannock

Art Unit

1646



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Dec 17, 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 22, 23, 25, 26, and 28-48 is/are pending in the application.
- 4a) Of the above, claim(s) 30-32, 38, and 40-46 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 22, 25, 28, 29, 33-37, 39, 47, and 48 is/are rejected.
- 7) ☒ Claim(s) 23 and 26 is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on Jun 11, 1999 is/are a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- *See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 4 6) ☐ Other:

Art Unit: 1646

DETAILED ACTION

Status of Application: Claims and Amendments

1. Applicant is notified that the amendments put forth in Paper 7, 6/11/1999, and in Paper 12, 9/3/02, and in Paper 15, 12/17/02, have been entered in full.
2. Claims 22, 23, 25, 26, 28-48 are pending.
3. Claims 30-32, 38, 40-46 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 12. Applicant's arguments regarding the species of SEQ ID NO: 1, 2, 13, and 14 are persuasive; thus the claims of Group I will be examined with respect to SEQ ID NO: 1, 2, 13, and 14. Further, as these claims appear to be free of the prior art, new claims 47 and 48 are being examined as well.

Priority

4. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. § 119(a)-(d) or § 365 as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)).

Art Unit: 1646

Drawings

5. The drawings are objected to as set forth in the attached PTO-948. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance. Additionally, Applicant is reminded that the Brief Description of the Drawings must refer to each part of a Figure; for example the specification should refer to Figure 19A-F, as purposed by the Draftsperson. Appropriate correction is required.

Specification

6. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reasons: Figures 22 and 24 make reference to specific polynucleotide and polypeptide sequences; these references must contain a sequence identifier of the form: SEQ ID NO: X. The sequence identifier may be located in either the figure itself or in the Brief Description of the Figures. Appropriate correction is required.

Art Unit: 1646

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 28, 39, 47 and 48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 28, 47 and 48 claims require that the nucleic acid hybridize to a reference nucleic acid. The term “hybridize” encompasses hybridization under conditions of varying degrees of stringency - such conditions determining the bounds of the claim. It is suggested that the claim recite the actual conditions that applicant considers to define the invention, i.e., salt concentration and temperature conditions of incubations and washes.

Claim 39 requires an assay comprising the step of measuring an appropriate transduction signal. The specification has not taught what transduction signal is appropriate. Furthermore, the claims do not present a step or steps to follow that would lead back to and accomplish the goal of the method that is recited in the preamble of the claim, i.e. it is unclear how the goal of assaying a substance for agonist or antagonist activity is to be accomplished. Thus the meets and bounds of the claim cannot be determined.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

Art Unit: 1646

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claim 39 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 39 requires an assay comprising the step of measuring an appropriate transduction signal.

The specification has not taught what transduction signal is appropriate. Thus the skilled artisan would not know how to practice the claimed invention.

11. Claims 22, 25, 29, 33, 34, 36, 37, 47 and 48 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polynucleotides encoding a protein of SEQ ID NO: 14 and the portion thereof capable of binding ICYP i.e. SEQ ID NO: 1, does not reasonably provide enablement for polynucleotides that do not encode a polypeptide of SEQ ID NO: 14.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification asserts that a polypeptides of SEQ ID NO: 1 and 14 are capable of binding ICYP and are thus useful in the study of ICYP transduction and drug development, yet

Art Unit: 1646

the claims claim a vast genus of polynucleotides that do not encode either SEQ ID NO: 1 or 14. The claims encompass polynucleotides encoding polypeptide variants of the polypeptide of SEQ ID NO: 14, i.e. substitutions, deletions or insertions in a protein corresponding to SEQ ID NO: 14. Applicant has not provided sufficient guidance as to how to make and use the encoded polypeptides which are not 100% identical to the polypeptide of SEQ ID NO: 14, but which still retain a desired property of the polypeptide of SEQ ID NO: 14. The claims require polypeptides comprising only portions of SEQ ID NO: 14, e.g. those comprising the formula sequence recited in claim 22 or polynucleotides that may only hybridize to polynucleotide encoding of SEQ ID NO: 14 or to only a portion of such a polynucleotide, e.g. claims 47 and 48. Thus, the vast majority of encoded polypeptides are amino acid sequence variants of SEQ ID NO: 14, i.e. amino acid substitutions, deletions or insertions in a protein corresponding to SEQ ID NO: 14, yet the specification has failed to teach one of skill in the art which amino acid substitutions, deletions or insertions to make. Furthermore, the Applicant has not provided guidance as to what properties of the allelic variants or sequence variants of the protein corresponding to SEQ ID NO: 14 might be desired nor any guidance as to which amino acid substitutions, deletions or insertions to make to achieve any desired property. Applicant has not defined a difference in structure or difference in function between the protein corresponding to SEQ ID NO: 14 and variants of said protein. If a variant of the protein corresponding to SEQ ID NO: 14 is to have a structure and function similar to the protein corresponding to SEQ ID NO: 14, then the specification has failed to teach one of skill in the art which amino acid substitutions, deletions or

Art Unit: 1646

insertions to make that will preserve the structure and function of the protein corresponding to SEQ ID NO: 14. Conversely, if a protein variant of SEQ ID NO: 14 need not have a disclosed property, the specification has failed to teach how to use such a variant. The specification has not provided a working example of the use of a variant of the polypeptide of SEQ ID NO: 14 nor sufficient guidance so as to enable one of skill in the art to make such a variant.

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These regions can tolerate only relatively conservative substitutions or no substitutions (see Bowie et al., 1990, Science 247:1306-1310, especially p.1306, column 2, paragraph 2). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Also, these or other regions may be critical determinants of antigenicity. It is well appreciated in the art of antibody production that it is

Art Unit: 1646

unpredictable which amino acids are critical antigenic determinants (see Alexander et al., Proc. Natl. Acad. Sci. 89(3352-3356)1992. Protein antigenicity can be significantly reduced by substitution of even a single residue. Further, even if an amino acid substitution does not destroy the activity of the immunizing protein, the substitution may significantly reduce the antigenicity of the protein (see the Abstract of Alexander et al.). The specification does not provide sufficient guidance as to how to make antibodies that are specific to variants of SEQ ID NO: 14 that can be used for any specific purpose. The specification has not provided guidance as to natural variants that may exist, nor how to use antibodies specific to variants that might be created.

Although the specification outlines art-recognized procedures for producing variants, this is not adequate guidance as to the nature of active variants that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity.

The specification has also failed to teach where to look for naturally occurring allelic variants of SEQ ID NO: 14, e.g. no disorder or phenotype has been asserted to correlate with a naturally occurring allelic variant, such that the artisan might now where to obtain a variant. The

Art Unit: 1646

specification merely offers the skilled artisan the invitation to randomly try to find variants through trial and error sampling of animal populations.

Due to the large quantity of experimentation necessary to generate the infinite number of variant recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

12. Claims 22, 25, 29, 33, 34, 36, 37, 47 and 48 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses a polynucleotide of SEQ ID NO: 13, yet the claims encompass polynucleotides not described in the specification, i.e. polynucleotides which comprise only portions of SEQ ID NO: 13, e.g. sequences from other species, mutated sequences, allelic

Art Unit: 1646

variants, or sequences that might hybridize to a portion of SEQ ID NO: 13. None of these sequences meet the written description provision of 35 U.S.C. 112, first paragraph. Although one of skill in the art would reasonably predict that these sequences exist, one would not be able make useful predictions as to the nucleotide positions or identities of those sequences based on the information disclosed in the specification.

The instant disclosure of a single polynucleotide, that of SEQ ID NO: 1, and a single portion thereof SEQ ID NO: 2, does not adequately support the scope of the claimed genus, which encompasses a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co*, 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. The instant specification discloses, however, a single isolated polynucleotide sequence SEQ ID NO: 13, which is not sufficient to describe the essentially limitless genera encompassed by the claims.

Thus, with the exception of the of the polynucleotide of SEQ ID NO: 1 and 13, and other polynucleotides which encode a polypeptide of SEQ ID NO: 14, the skilled artisan cannot envision encompassed variants. Therefore, only polynucleotides encoding a polypeptide of SEQ ID NO: 14, and polynucleotides *consisting* of fragments thereof, or polynucleotides consisting of

Art Unit: 1646

fragments thereof and heterologous sequences (e.g. carrier or tag sequences), but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph.

13. Claim 35 is rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The invention appears to employ novel nucleic acid molecules (i.e. that deposited as CNCM No. I-1795). Since the nucleic acid molecules are essential to the claimed invention they must be obtainable by a repeatable method set forth in the specification or otherwise readily available to the public. If the nucleic acid molecules are not so obtainable or available, the requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the nucleic acid molecules. The specification does not disclose a repeatable process to obtain the nucleic acid molecules and it is not apparent if the nucleic acid molecules are readily available to the public. It is noted that Applicant has deposited the nucleic acid molecules (page 5), but there is no indication in the specification as to public availability. If the deposit is made under the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific nucleic acid molecules have been deposited under the Budapest Treaty and that the nucleic acid molecules will be irrevocably and without restriction or condition released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. If the deposit has not been made under the

Art Unit: 1646

Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 C.F.R.

§§ 1.801-1.809, Applicant may provide assurance of compliance by an affidavit or declaration, or

by a statement by an attorney of record over his or her signature and registration number,

showing that:

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;

(d) a test of the viability of the biological material at the time of deposit will be made (see 37 C.F.R. § 1.807); and

(e) the deposit will be replaced if it should ever become inviable.

Allowable Subject Matter

14. Claims 23 and 26 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Art Unit: 1646

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (703) 306-5876. The examiner can normally be reached on Mondays through Thursdays from 8:00 a.m. to 5:30 p.m. The examiner can also normally be reached on alternate Fridays.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

March 20, 2003


YVONNE EYLER, PH.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600